AD-A107 907 LETTERMAN ARMY INST OF RESEARCH PRESIDIO OF SAN FRANC--ETC F/G 6/20
PRIMARY DERMAL IRRITATION POTENTIAL OF COMPONENTS OF THE M-258A--ETC(U)
SEP 81 J T FRUIN, M A HANES
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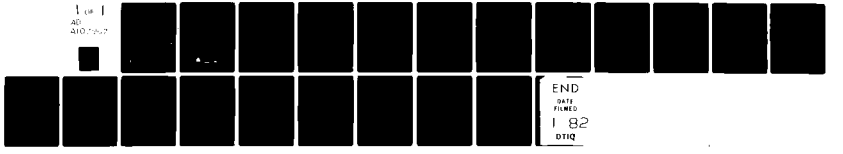

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REPORT DOCUMENTATION PAGE

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1. REPORT NUMBER: LAIR Technical Note No. 81-22TN
2. GOVT ACCESSION NO.: AD-A107907
3. RECIPIENT'S CATALOG NUMBER:

4. TITLE *(and Subtitle)*: Primary Dermal Irritation Potential of Component of the M-258 Decontamination Kit (Study 3)
5. TYPE OF REPORT & PERIOD COVERED: Final, 4 June 1981 - 29 June 1981
6. PERFORMING ORG. REPORT NUMBER:

7. AUTHOR(s): John T. Fruin, DVM, PhD, LTC VC; Martha A. Hanes, DVM, CPT VC
8. CONTRACT OR GRANT NUMBER(s):

9. PERFORMING ORGANIZATION NAME AND ADDRESS: Toxicology Group, Div. of Research Support, Letterman Army Institute of Research, Presidio of San Francisco, CA 94129
10. PROGRAM ELEMENT, PROJECT, TASK AREA & WORK UNIT NUMBERS: Project 35162772.875, WU 302

11. CONTROLLING OFFICE NAME AND ADDRESS: U.S. Army Medical Research and Development Command, Fort Detrick, Frederick, MD 21701
12. REPORT DATE: September 1981
13. NUMBER OF PAGES: 20

14. MONITORING AGENCY NAME & ADDRESS *(if different from Controlling Office)*:
15. SECURITY CLASS. *(of this report)*: UNCLASSIFIED
15a. DECLASSIFICATION/DOWNGRADING SCHEDULE:

LEVEL II

16. DISTRIBUTION STATEMENT *(of this Report)*

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18. SUPPLEMENTARY NOTES

19. KEY WORDS *(Continue on reverse side if necessary and identify by block number)*

M-258 Kit, Primary Dermal Irritation Chemical Defense, Chemical Decontamination.

20. ABSTRACT *(Continue on reverse side if necessary and identify by block number)*

The dermal irritation potential of components of the Prototype M-258A-1 Decontamination Kit was assessed by using a modified Draize test. The test called for approximately 0.04 g of freshly prepared material to be held in contact with the skin of rabbits for 24 hr. Both components, Decon I and Decon II when applied separately and together, caused little irritation after exposure for 24 hr. Further testing of these components is recommended to determine if they present a significant hazard under field conditions.

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TECHNICAL NOTE NO. 81–22TN

PRIMARY DERMAL IRRITATION POTENTIAL OF COMPONENTS OF THE M-258A-1 DECONTAMINATION KIT (Study 3)

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and
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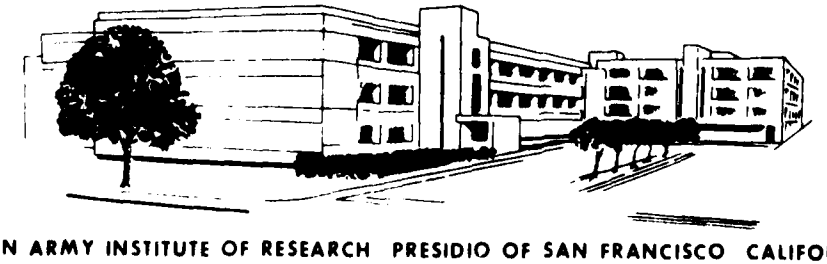
TOXICOLOGY GROUP,
DIVISION OF RESEARCH SUPPORT

SEPTEMBER 1981 **Toxicology Series 9**



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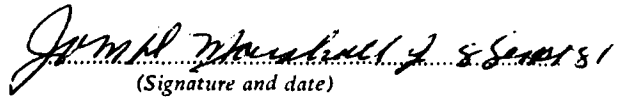
Toxicology Series 9

In conducting the research described in this report, the investigation adhered to the "Guide for the Care and Use of Laboratory Animals," as promulgated by the Committee on Revision of the Guide for Laboratory Animal Facilities and Care, Institute of Laboratory Animal Resources, National Research Council.

This material has been reviewed by Letterman Army Institute of Research and there is no objection to its presentation and/or publication. The opinions or assertions contained herein are the private views of the author(s) and are not to be construed as official or as reflecting the views of the Department of the Army or the Department of Defense. *(AR 360-5)*



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PREFACE

Primary Dermal Irritation GLP Study Report

TESTING FACILITY: Letterman Army Institute of Research
Presidio of San Francisco, CA 94129

SPONSOR: Letterman Army Institute of Research
Presidio of San Francisco, CA 94129

PROJECT: Medical Defense Against Chemical Agents 612772.875.

GLP STUDY NUMBER: 81019

STUDY DIRECTOR: LTC (P) John T. Fruin, DVM, PhD, VC, Diplomate of American College of Veterinary Preventive Medicine

PRINCIPAL INVESTIGATOR: CPT Martha A. Hanes, DVM,VC

RAW DATA: A copy of the final report, study protocol, raw data, and standard operating procedures will be retained in the LAIR Archives.

TEST SUBSTANCES:

A. Freshly prepared Decon I consists of hydroxyethane (ethanol) 72 $\pm$ 2% phenol 10 $\pm$ 0.5%, sodium hydroxide 5 + 0.5%, ammonium hydroxide 0.2 $\pm$ 0.05% and water.

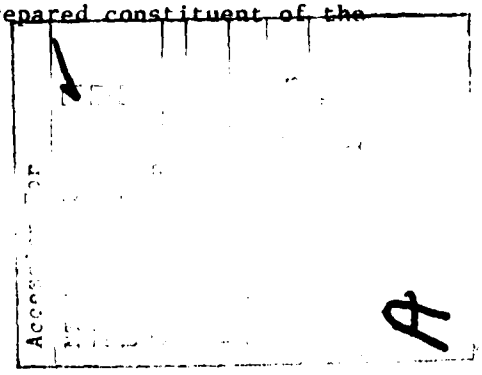
B. Freshly prepared Decon II consists of crystalline chloramine B and an equal quantity of liquid. The liquid containes hydroxyethane (ethanol) 45 $\pm$ 2%, zinc chloride 5$\pm$0.5% and water. Just prior to dosing, the chloramine B and liquid are mixed together.

C. Decon I and Decon II combined.

D. Control (dry 1 inch square cotton gauze pad)

WORK UNIT: 302 Studies on Potential Dermal Irritation of M-258 Kit

PURPOSE: The purpose of this study was to determine the primary dermal irritation potential of freshly prepared constituent of the M-258A-1 Decontamination Kit.



ACKNOWLEDGMENTS

The authors wish to thank LTC Kenneth Black MD, MC; CPT Warren Jederberg, MS; SSG Dennis Smith; SSG Lance White; SP4 Thomas Kellner, BA; PFC Evelyn Zimmerman; and Carolyn Lewis, MS; for assistance in preforming the research, and for advice in scoring the irritation reactions. The authors also wish to thank LTC (P) E. Houston, PhD, MS; LTC R. Howarth, VMD, VC; M. Mershon, VMD; of the U.S. Army Medical Institute of Chemical Defense, Aberdeen Proving Grounds, Edgewood Arsenal, MD, for providing background information.

Signatures of Principal Scientists Involved
In The Study

We, the undersigned, believe the study, GLP number 81019, described in this report to be scientifically sound and the results and interpretation to be valid. The study was conducted to comply, to the best of our ability, with the Good Laboratory Practice Regulations for Nonclinical Laboratory Studies outlined by the Food and Drug Administration.

Martha A. Hanes 21 Aug 81
MARTHA A. HANES, DVM / DATE
CPT, VC
Principal Investigator

John T. Fruin 2 Sept 81
JOHN T. FRUIN, DVM, PhD / DATE
LTC (P), VC
Study Director

DEPARTMENT OF THE ARMY
LETTERMAN ARMY INSTITUTE OF RESEARCH
PRESIDIO OF SAN FRANCISCO, CALIFORNIA 94129

REPLY TO ATTENTION OF

SGRD-ULZ-QA

22 July 1981

MEMORANDUM FOR RECORD

SUBJECT: Report of GLP Compliance

I hereby certify that in relation to LAIR GLP study 81019 the following inspections were made:

11 June 1981
15 June 1981
16 June 1981
18 June 1981

Routine inspections with no adverse findings are reported quarterly, thus these inspections are also included in the July 1981 report to management and the Study Director.

JOHN C. JOHNSON
CPT, MS
Quality Assurance Officer

PRIMARY DERMAL IRRITATION POTENTIAL OF COMPONENTS
OF THE M-258A-1 DECONTAMINATION KIT (Study 3)

An evaluation of the Prototype M-258A-1 Decontamination Kit for primary dermal irritation potential by using the modified Draize test (1) was recently completed (2). That evaluation produced evidence of severe irritation potential. Further testing was deemed necessary to determine the kits irritation potential using freshly prepared material. The reason for this was to insure that dermal irritation was not the result of chemical deterioration.

Deviation from standards

Rather than applying 0.5 ml of liquid test substance, the amount was reduced to the amount needed to wet on square inch of close clipped rabbit skin.

Chemical analysis were not conducted except for measuring pH. Purity is unknown. Chemicals were prepared in accordance with the components and concentrations available from the M-258A-1 Kit Manufacters. Division of Cutaneous Hazards was responsible for the preparation. Tables 1 and 2 list the components and their concentration. Freshly prepared compounds are assumed to be stable, for the duration of the test, but no tests were conducted.

TABLE 1 (3)

CHEMICAL ANALYSIS OF DECON I
(pH = 10.6 - 10.7)

Component	ETOH	H_2O	Phenol	NaOH	NH_4OH
%	72%±2%	q.s.	10±0.5%	5.0±0.5%	0.2±0.05%
Name	ethanol	water	phenol	sodium hydroxide	ammonium hydroxide
Molecular Structure	C_2H_6O	H_2O	C_6H_6O	NaOH	NH_4OH
Molecular Weight	46.07	18.016	94.12	40.01	35.036

TABLE 2 (3)

CHEMICAL ANALYSIS OF DECON II
(pH = 6.1 - 6.2)

	*LIQUID PORTION			*SOLID PORTION
Component	ETOH	H_2O	$ZnCl_2$	Chloramine B
%	45±2%	50±2.5%	5±0.5%	100%
Name	ethanol	water	zinc chloride	Chloramine B (N-Chlorobenzene-sulfamido-sodium)
Molecular Structure	C_2H_6O	H_2O	ZnI_2	C_6H_5Cl $NNaO_2S$
Molecular Weight	46.07	18.016	136.29	213.64

* Equal quantities of liquid and solid are mixed to form Decon II.

Objective of Study

The objective of this study was to determine the primary dermal irritation potential of freshly prepared compounds used in the M-258

Decontamination Kit. The quantity of material used was that needed to wet a one-square-inch area of clipped rabbit skin.

METHODS

Historical Listing of Study Events

4 June 1981	Animals were clipped and held for study.
9 June 1981	Animals were weighed.
11 June 1981	Sites for exposure were randomized. Animals were clipped and areas marked.
15 June 1981	Animals were dosed and weighed.
15-29 June 1981	Animals were observed daily, only significant or abnormal observations were recorded.
16 June 1981	Bandages removed, 24-hr post-exposure score.
18 June 1981	72-hr post-exposure score.
22 June 1981	7-day post-exposure score, weight taken.
29 June 1981	Animals were scored (14-day post-exposure) and weights taken. Animals were removed from the study.

Animal Data

Animal: New Zealand White Rabbits

Sex: Male

Source: Elkhorn Rabbitry

Pre-test Conditioning:

A. Transferred from GLP Study 81005, a primary eye irritation study. Animals were rested for 3 weeks after the last eye treatment

B. Animals were close clipped and test areas marked

Method of Randomization: Manual, Latin Square, SOP-OP-STX-34

Number of Animals on test: 6 animals - each animal had 4 test sites and received each of the three test treatments and a control with no treatment

Age of animals at start of study: young adults

Body Weight Range: 3-4 kg

Condition of animals at start of study: normal

Identification System: Ear marked as per SOP-OP-AGR-1

Environmental Conditions

Caging: Number/cage = 1; Type cage used = stainless steel, wire mesh bottom, battery type, no bedding, automatic flushing

Diet: Purina Certified Rabbit Chow 5322 approximately 110 g per day supplemented with about 45 g of fresh carrots

Water: Central line to cage battery with automatic lick dispensers

Temperature: 75 ± 5 F (24 ± 3 C)

Relative Humidity: 50 ± 10%

Photoperiod: 0530 - 2000 hr/day (14 1/2 hr of light)

Dosing Levels

A. Decon I: 0.04 ml

B. Decon II: 0.04 ml

C. Decon I and II: 0.02 ml and 0.02 ml, respectively

D. Control: A dry square inch gauze pad was taped to the animal.

Dosing Procedures

Method and frequency of administration were dictated by SOP-OP-STX-34. The backs of the animals were close clipped and divided into quadrants designated I,II,III and IV. Areas I and IV

were intact on all animals, and areas II and III were abraded by making two perpendicular scratches in the stratum corneum of the skin about 1 1/2 inch long by using an escarifier. The four application sites were about 10 cm apart. A standard latin square table was used to randomize the test sites (SOP-OP-STX-34).

The test substance impregnated pads were wiped over the test sites. A plastic strip held on by elastic tape was placed around the animal to retard evaporation, and to insure skin contact by the test substance. The test substance was in contact with the skin for 24 hours. At the end of the exposure period the wrapping was removed, the skin wiped if material was adherent and scored.

RESULTS

Scoring

Six animals were exposed to the chemicals. Animals were scored at 24 and 72 hr, 7 and 14 days for edema/erythema (Table 3). Tabular data appear in Appendix A. Abraded areas (sites II and III) and intact areas (sites I and IV) were graded separately as well as together. The scores obtained were used for a basis for categorization. Primary irritation potential values were calculated from the 24-and 72-hr scores.

TABLE 3

EVALUATION OF SKIN REACTIONS (4)

Erythema and Eschar Formation	
No erythema	0
Very slight erythema (barely perceptible)	1
Well defined erythema	2
Moderate-to-severe erythema	3
Severe erythema (beet redness) to slight eschar formation (injurious in depth)	4
Possible total erythema score	4*
Edema Formation	
No edema	0
Very slight edema (barely perceptible)	1
Slight edema (edges of area well defined by definite raising)	2
Moderate edema (edges raised aproximately 1 mm)	3
Severe edema (raised more than 1 mm and extending beyond area of exposure)	4
Possible total edema score	4*
Possible total score for primary irritation	8

* Any skin reaction more serious than severe erythema, severe edema, vesiculation, ulceration, or necrosis places the chemical in Category IV.

Table 4 demonstrates the primary irritation indexes for the exposed areas.

TABLE 4

PRIMARY DERMAL IRRITATION INDEX FOR M-258A-1 DECONTAMINATION KITS

Chemical	Intact Score	Abraded Score	Combined Score	Category
Decon I	0.5	0.83	0.67	I
Decon II	0.0	0.5	0.25	I
Decon I+II	0.33	0.08	0.25	I
Control	0.17	0.17	0.17	I

DISCUSSION

Decon I, and II separately, and combined were significantly less irritating when applied in appropriate quantities expected under field conditions. Compounds producing combined averages of 2 or less are considered non-irritating (provided the intact score is by itself less than 0.5) and placed in Category I.

In the study, the quantity of material used to dose was the amount needed to wet one-square-inch of clipped skin absorbed on a cotton gauze pad. Some of the compound is trapped in the cotton gauze material and is not in contact with the skin. Results from simulated usage should be given more consideration in the evaluation of the kit.

CONCLUSIONS

The modified Draize test demonstrated the irritation potential

of the Prototype M-258A-1 Decontamination Kit Components, when freshly prepared, are less irritating when applied in a lower quantity. This supports the possibility of compound instability. Damage may have been produced by some breakdown product in earlier studies conducted (see Toxicology Series 6). The effect of age on the components should be scrutinized.

RECOMMENDATIONS

Recommendations will be made after the current series of studies is completed.

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Summary of Primary Skin Irritation Test Data

APPENDIX A

APPENDIX A-I

Summary of Primary Skin Irritation Test Data

GLP Study No. 81019	Chemical Name	Conc	Solvent	Amt Applied	Code
Date of Application 15 June 1981	Decon I	100%	NA	0.4 ml	A

Principal Investigator CPT HANES

Irritation Scores

		Intact Skin Sites				Abraded Skin Sites				
Rabbit No.	Site	Erythema 24 hr	Erythema 72 hr	Edema 24 hr	Edema 72 hr	Site	Erythema 24 hr	Erythema 72 hr	Edema 24 hr	Edema 72 hr
F8100043	I	0	0	0	0					
F8100050	IV	0	0	0	0					
F8100051						III	1	2	0	0
F8100055						II	1	1	0	0
F8100056	I	0	0	2	1					
F8100075						III	0	0	0	0
Total:		a 0	b 0	a 2	b 1		a 2	b 3	a 0	b 0
		a+b 0		a+b 3			a+b 5		a+b 0	
		C^I 3					C^A 5			

Intact Score = C^I / 2xNo. of Sites on test 3/(2x3) = 0.5

Abraded Score = C^A / 2xNo. of Sites on test 5/(2x3) = 0.83

Total Score = $\frac{C^I+C^A}{2}$ x No. of Sites on test 8/(2x6) = 0.67

Primary Skin Irritation Index Category I

Remarks:

APPENDIX A-2

Summary of Primary Skin Irritation Test Data

GLP Study No. 81019 Chemical Name | Conc | Solvent | Amt Applied | [illegible]

Date of Application 15 June 1981 | Decon II | 100 | NA | 0.4 ml | [illegible]

Principal Investigator CPT HANFS

Irritation Scores

		Intact Skin Sites					Abraded Skin Sites				
Rabbit No.	Site	Erythema 24 hr	Erythema 72 hr	Edema 24 hr	Edema 72 hr	Site	Erythema 24 hr	Erythema 72 hr	Edema 24 hr	Edema 72 hr	
F8100043						II	1	1	0	0	
F8100050	I	0	0	0	0						
F8100051	IV	0	0	0	0						
F8100055						III	0	0	0	0	
F8100056						II	0	1	0	0	
F8100075	I	0	0	0	0						
Total:		a 0	b 0	a 0	b 0		a 1	b 2	a 0	b 0	
		a+b 0		a+b 0			a+b 3		a+b 0		
				C^I 0					C^A 3		

Intact Score = C^I / 2xNo. of Sites on test 0/(2x3) = 0.0

Abraded Score = C^A / 2xNo. of Sites on test 3/(2x3) = 0.5

Total Score = $\frac{C^I+C^A}{2 \times \text{No. of Sites on test}}$ 3/(2x6) = 0.25

Primary Skin Irritation Index Category I

Remarks:

APPENDIX A-3

Summary of Primary Skin Irritation Test Data

GLP Study No. 81019	Chemical Name	Conc	Solvent	Amt Applied	Case
Date of Application 15 June 1981	Decon I + II	100%	NA	0.02 ml I 0.02 ml II	C

Principal Investigator CPT HANES

Irritation Scores

		Intact Skin Sites					Abraded Skin Sites				
Rabbit No.	Site	Erythema 24 hr	Erythema 72 hr	Edema 24 hr	Edema 72 hr	Site	Erythema 24 hr	Erythema 72 hr	Edema 24 hr	Edema 72 hr
F8100043						III	0	0	0	0
F8100050						II	0	1	0	0
F8100051	I	0	0	0	0					
F8100055	IV	1	1	0	0					
F8100056						III	0	0	0	0
F8100075	IV	0	0	0	0					
Total:		a 1	b 1	a 0	b 0		a 0	b 1	a 0	b 0
		a+b 2		a+b 0			a+b 1		a+b 0	
		C^I = 2					C^A = 1			

Intact Score = C^I / 2xNo. of Sites on test 2/(2x3) = 0.33

Abraded Score = C^A / 2xNo. of Sites on test 1/(2x3) = 0.17

Total Score = $\frac{C^I+C^A}{2}$ x No. of Sites on test 3/(2x6) = 0.25

Primary Skin Irritation Index Category I

Remarks:

APPENDIX A-4

Summary of Primary Skin Irritation Test Data

GLP Study No. 81019 | Chemical Name | Conc | Solvent | Amt Applied | Time

Date of Application 15 June 1981 | Control | | | | 0

Principal Investigator CPT HANES

Irritation Scores

		Intact Skin Sites					Abraded Skin Sites				
Rabbit No.	Site	Erythema 24 hr	Erythema 72 hr	Edema 24 hr	Edema 72 hr	Site	Erythema 24 hr	Erythema 72 hr	Edema 24 hr	Edema 72 hr	
F8100043	IV	0	0	0	0						
F8100050						III	0	0	0	0	
F8100051						II	1	0	0	0	
F8100055	I	0	0	0	0						
F8100056	IV	1	0	0	0						
F8100075						II	0	0	0	0	
Total:		a 1	b 0	a 0	b 0		a 1	b 0	a 0	b 0	
		a+b 1		a+b 0			a+b 1		a+b 0		
		C^I = 1					C^A = 1				

Intact Score = C^I / 2xNo. of Sites on test 1/(2x3) = 0.17

Abraded Score = C^A / 2xNo. of Sites on test 1/(2x3) = 0.17

Total Score = $\frac{C^I+C^A}{2 \times \text{No. of Sites on test}}$ 2/(2x6) = 0.17

Primary Skin Irritation Index Category I

Remarks: